Author's response to reviews

Title: Evaluation of symptomatic slow-acting drugs in osteoarthritis using the GRADE system

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Dear Editor,

Please find enclosed our manuscript entitled “Evaluation of symptomatic slow-acting drugs in osteoarthritis using the GRADE system”, that we would like to submit to BMC Musculoskeletal Disorders for publication.

As previously requested, you will find below a point by point response to the reviewers comments.

Reviewer 1

The research question is of great interest and worthwhile to be discussed. This manuscript constitutes a kind of a meta-analysis of meta-analyses. The authors state that only outcome parameters, appraised as important (VAS>6) are included into the evaluation. It would be interesting to see the results of this procedure and the heterogeneity of judgements across the groups. To the reviewer’s opinion the interpretations are overly positive particularly with respect to Glucosamine. There should be an explanation included why the recommendation for Glucosamin is stronger than for the other compounds. The positive results for Glucosamin derive primarily from studies with one product from one company. Some remarks concerning the results of the GAIT trial should be included into the discussion section.

Authors: Recommendations are mainly based on the most recent meta-analysis based on pivotal studies. Pivotal trials are high-quality studies used by Health Authorities to assess the efficacy and safety of a prescribed medication in order to grant the marketing authorisation. The GAIT trial has been discussed in the “discussion” section.

Methods seem to be well described and also well chosen. As with all the other systems to assess strength of recommendation also the GRADE format is very
much focused on literature results. A description of the experts’ opinion, e.g. by a VAS or a Likert scale, within the group could help to provide higher transferability into daily routine, as it would give an impression of interindividual variance between the group.

Authors: we agree that our text was not very clear. As a matter of fact, outcomes considered as important must be scored >6mm (on a 10mm VAS) by all experts. The paragraph has been modified.

The manuscript adheres to relevant standards for reporting and data deposition. The title and abstract are accurately formulated. The writing, organization, tables and figures are descriptive and well chosen.

Authors: we thanks the reviewer. However, as suggested by reviewer 3, our title has been modified.

As most of the authors are well known experts in the field of OA their relationship to the relevant companies, e.g. involvement in clinical trials, steering committees, speakers bureaus etc. should be given.

Authors: a competing interest section has been added in the manuscript.

Reviewer 2

The authors are submitting an … intriguing manuscript. Based on the title, the reader is not aware whether it will be a review, a systematic literature research, a meta-analysis or a recommendation paper… I have to recognize that this question is still accurate … after the reading of the manuscript.

Authors: as also suggested by reviewer 3, our title has been changed

If we consider that the objective was to conduct a systematic literature research, several important items are missing in the Methods section and, in particular: the date of the research, the evaluated database, the exact key words (the reviewer has not understood the methodology used in order to select the drugs), the Outcome measures (function? Pain? Structure? …)

Authors: more information has been provided in the methods section of the manuscript. As a matter of fact, systematic and exhaustive search of the meta-analysis and randomized controlled trials published from 1950 until December 2007 has been undertaken, using several tools, such as Medline, Old Medline, Embase, CINAHL, Science Citation Index through Web of Science, Allied Complementary Medicine and Cochrane Library databases. The search in the Cochrane Library included the Cochrane Reviews, Abstracts of Quality Assessed Systematic Reviews, The Cochrane Controlled Trial Register, NHS Economic Evaluation Database, Health Technology Assessment Database and NHS Economic Evaluation Bibliography Details Only. Outcome measure has been specified in the results section.

If we consider that the objective was to propose recommendations (as stated in the introduction), the authors should revise their manuscript with regard to the recent OARSI publication.
Authors: it should be pointed out that our expert meeting has been conducted before the publication of the OARSI recommendations and that they do not use the GRADE system. However, we have added this publication in our references.

Reviewer 3

This is a recommendation document based on systematic review of Drug Trials in OA by a selected group of ESCEO experts - who happen to be in the mainly osteoporosis experts. The conclusions are that most drugs and supplements tested could be of use in the management of OA. There are a number problems with the recommendations.

1. It does not read well - and is clearly not written or edited by English speaker.
   Authors: the manuscript has been reviewed.

2. More tables and less text would be appropriate.
   Authors: We believe that all the information that we have provided in the text could hardly be summarized in a table. We respectfully suggest to keep our text.

3. The use of risk benefit ratio has some merits - but needs validation.
   Authors: we agree with the reviewer and it has been added as a limitation of this study.

4. The studies were not blinded and experts reviewed the quality of their own work or reviews.
   Authors: we also agree with the reviewer and it has been added as a limitation of this study.

5. The panel would not be considered a representative panel of OA treatment experts.
   Authors: we agree with the reviewer. However, some guideline experts suggest the inclusion of non-expert in the field when producing recommendation.

6. The review does not consider the source of funding for the studies as an issue.
   Authors: we agree with the reviewer and it has been added in the manuscript.

7. Individual ratings should be shown.
   Authors: the GRADE recommendation is reached by consensus and not by individual rating. It has been added in the text.

8. Unclear who is intended reader.
   Authors: intended readers have been added.

We hope to have provided appropriate response and would like to thank you in advance for the care taken in reviewing our manuscript.

Sincerely yours,
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